ABSTRACT OF THE INVENTION

Co-incubation of an amyloid protein with sulfated macromolecules as a method for the formation of amyloid plaques. The amyloid protein may be the beta-amyloid protein or the prion protein or the like. Amyoid plaque formation in one embodiment proceeds *in vitro* and desireably produces amyloid plaques that stain with Congo red and demonstrate a maltese-cross pattern when viewed under polarized light. The method also produces amyloid plaques that demonstrate an "amyloid star" appearance when viewed by transmission electron microscopy.

Sulfated macromolecules include a sulfated proteoglycan selected from the group consisting of perlecan, ~220 kilodalton heparan sulfate proteoglycan, glypican, cerebroglycan, aggrecan, synaptoglycan (SV2PG), syndecan, N-syndecan (also known as syndecan-3), syndecan-1, syndecan-4, neurocan, phosphacan, decorin, biglycan, versican, amphiglycan, lumican, PG-M, PG-M (3), agrin, betaglycan, claustrin, brevican, appican, epican, neuroglycan-C, and fragments thereof. Thw sulfated macromolecule may be a sulfated glycosaminoglycan selected from the group consisting of heparin, heparan sulfate, dermatan sulfate, chondroitin sulfate, keratan sulfate, and fragments thereof.

An *in vivo* assay is also presented for selecting a candidate therapeutic agent for inhibiting or disrupting amyloid plaque deposition or persistence. The assay includes a) pre-forming congophilic maltese-cross amyloid plaques *in vitro* following incubation of an amyloid protein and a selected sulfated macromolecule, b) using a first cannula and osmotic pump to continuously infuse for a selected duration the pre-formed congophilic maltese-cross amyloid plaques into a tissue or organ, c) changing the first cannulae and osmotic pump with a second cannulae and osmotic pump to administer the candidate therapeutic, and d) detecting the candidate therapeutic's ability to disrupt, reduce, or eliminate congophilic maltese-cross amyloid plaque deposition/persistence in the tissue or organ.